Primary Smooth Muscle Tumors of Venous Origin

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Vein tumors are rare, difficult to diagnose, and usually malignant. We have encountered three: a leiomyoma of the jugular vein and leiomyosarcomas of the saphenous vein and inferior vena cava (IVC). The leiomyoma was lost to follow-up, the saphenous vein leiomyosarcoma survived nine years, and the leiomyosarcoma of the IVC is six months without recurrence. Half of venous leiomyosarcomas arise in the IVC, predominately in women over 50 years of age. Surgical excision is the treatment of choice since malignant or benign status cannot be determined operatively. Resection should include a segment of the original vessel. This poses problems in the IVC when the renal veins require sacrifice. Right renal vein interruption mandates nephrectomy. Edema following IVC resection is evaluated. The incidence is lower than anticipated when resection is for tumor if there is no history of phlebitis. The IVC was reconstructed with a composite autograft but this is not now recommended. Despite significant local recurrences or distal metastases, cure or long-term palliation can often be achieved. Radiation and chemotherapy do not improve survival or prevent recurrence.

PRIMARY SMOOTH muscle tumors of vascular origin are unusual. They may be either benign or malignant,[1] and may arise from any of the tissues of the vessel wall. They include endotheliomas from the intima,[2] fibrosarcomas from connective tissues,[3] and leiomyomyomas or leiomyosarcomas from the smooth muscle of the media.[4] These neoplasms have been reported to arise both in large arteries and veins,[5,6] but are five times more common in the latter.[7] Most tumors of blood vessel origin are malignant.

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In 1979, approximately 120 cases were recorded in the world literature.[4] Despite this rarity, the authors have encountered three such cases. Since experience with these lesions is limited, it is felt that they should be reported.

Case 1

A 75-year-old white female was admitted to the hospital in December 1975 with a one-week history of an enlarging but otherwise asymptomatic, left neck mass. Physical examination revealed a 3 × 4 cm nontender, immobile, nonpulsatile mass in the left upper jugular region. There was no overlying bruit. All studies done to determine a primary source for this mass were unrevealing. A preoperative diagnosis of chemodectoma or metastatic carcinoma was made. Upon exploration, the mass was found to be intimately attached to the upper end of the internal jugular vein, and was resected in continuity with the vein. On pathologic examination, the mass was reported to be a benign leiomyoma arising from the tunica media of the vein. The postoperative course was uneventful. When the patient was last seen two months after surgery, there was no evidence of recurrence.

Case 2

A 66-year-old black female noted an asymptomatic enlarging left groin mass in June 1965. She had been treated 30 years earlier for benign uterine disease with radium implantation. Examination revealed a hard 1.5 × 2.0 cm mass in the region of the left fossa ovalis. First consideration was that the mass was metastatic, but sigmoidoscopy, intravenous pyelogram, barium enema, and cystoscopy failed to reveal a primary site. Excisional biopsy of the mass was performed. Pathologic examination showed it to be metastatic leiomyosarcoma completely replacing lymph nodes. Suspecting a gynecologic primary, under anesthesia, a pelvic examination and dilatation and curettage were performed. This revealed several small uterine fibroids. Lymphangiography visualized lymphatics only up to the groin, in the area of surgery. Still suspecting the primary to be in the uterus, a total hysterectomy bilateral salpingo-oophorectomy and left radical pelvic and groin node dissection were performed, but failed to reveal a primary site in the uterus or adnexa. During the radical groin dissection, however, a tumor was found within the greater saphenous vein that protruded like a finger into the femoral vein at their junction. This tumor was resected by excision of the greater saphenous vein and tangential excision of the wall of the femoral vein, which was recon-

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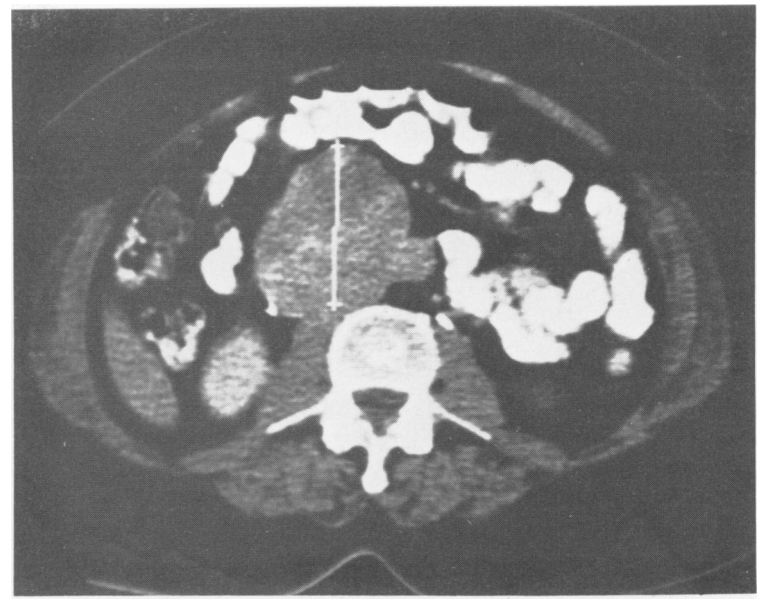


FIG. 1. Case 3—CT scan of abdomen showing large retroperitoneal mass adjacent to aorta. IVC not identifiable.

structed by lateral venorrhaphy. Pathologic examination of the specimen confirmed that the leiomyosarcoma arose from the saphenous vein.

After operation, the patient experienced moderate edema of the left lower extremity that was controlled by elastic stockings. She was free of recurrence when last seen four years later. She did not receive postoperative radiation or chemotherapy. Communication with the family revealed that she died in 1974, nine years after the original surgery. Spread of her disease was suspected as the cause of death, although postmortem examination was not performed.

Case 3

A 55-year-old black female was admitted to the hospital on June 3, 1981. She complained of intermittent right-sided abdominal pain radiating around the right flank for the past eight months and a 15-pound weight loss. Examination of the abdomen revealed a slightly tender, deep seated, 6- to 8-cm mass in the mid-epigastric region that was fixed and had no pulsations. White blood count on admission was 3,200, with 39% neutrophiles, 45% lymphocytes, 8% monocytes, 4% eosinophils and 3% atypical lymphocytes. Sonography revealed a solid echo-poor retroperitoneal mass measuring 7.5 × 7.5 × 4.5 cm and silhouetting the inferior vena cava below the level of the kidneys. Lymphadenopathy was suspected. Intravenous phelography showed lateral displacement of the right ureter by the mass. Barium enema was unremarkable, and an upper gastrointestinal series revealed anterior displacement of the descending portion of the duodenum and several duodenal diverticula. Computed tomography of the abdomen demonstrated a large retroperitoneal mass from L2 to the upper pelvis, that silhouetted the lower abdominal aorta and inferior vena cava. The mass was felt to represent enlarged retroperitoneal nodes (Fig. 1). Bone marrow biopsy was unrevealing. The patient was explored with a presumptive diagnosis of retroperitoneal lymphoma. At surgery, a huge 8 × 8 × 5 cm irregular firm, solid mass was found arising from the anterior wall of the infra-renal inferior vena cava, adherent to, but separable from the aorta and surrounding structures. It was resected in continuity with the infrarenal vena cava. The caval defect was bridged with a composite autograft, fashioned from both saphenous vein trunks, harvested from the groins.

After operation, she was placed on heparin and then switched to warfarin. To prevent lower extremity edema, she was fitted with compression bandages and elastic stockings and instructed to elevate her legs. Postoperative chemotherapy was considered but not given. She remained on warfarin for two months, doing well. She then discontinued both the medication and the elastic stockings of her own volition. After the immediate postoperative period, she exhibited no edema. There has been no recurrence of the mass thus far. A venogram done three and a half months after surgery showed complete occlusion of the caval graft but excellent collateral circulation (Fig. 2). Her postoperative white blood count returned to normal. Pathologic examination of the resected tumor disclosed a leiomyosarcoma with nuclear pleomorphism, numerous mitoses, and hypercellularity. It appeared to arise from the muscle layer, infiltrated the intima but did not disrupt the endothelium.

Discussion

The most common neoplasm of vascular origin is the leiomyosarcoma. In about half of the recorded cases (62/120) the primary site has been reported to be the inferior vena cava,[8] and next in frequency are those arising in the long saphenous vein (approximately 25%). The remainder of the venous neoplasms come from various vessels throughout the body,[5,6,9] including the femoral vein, internal jugular, and iliac vein in descending order. There is a predilection for veins of the lower extremities.

Leiomyosarcomas arising in the inferior vena cava are more commonly found in women over the age of 50 (80% of reported cases). However, when these neoplasms arise in other large veins, 66% affect men and only 33% women. Leiomyosarcomas in major arteries show an approximately equal sex distribution.

Prior to recent advances in diagnostic radiology, most cases were diagnosed at autopsy. In the past 15 years, however, many cases arising from the inferior vena cava and other major vessels have been diagnosed before operation or at surgery.

It is impossible to determine whether these tumors

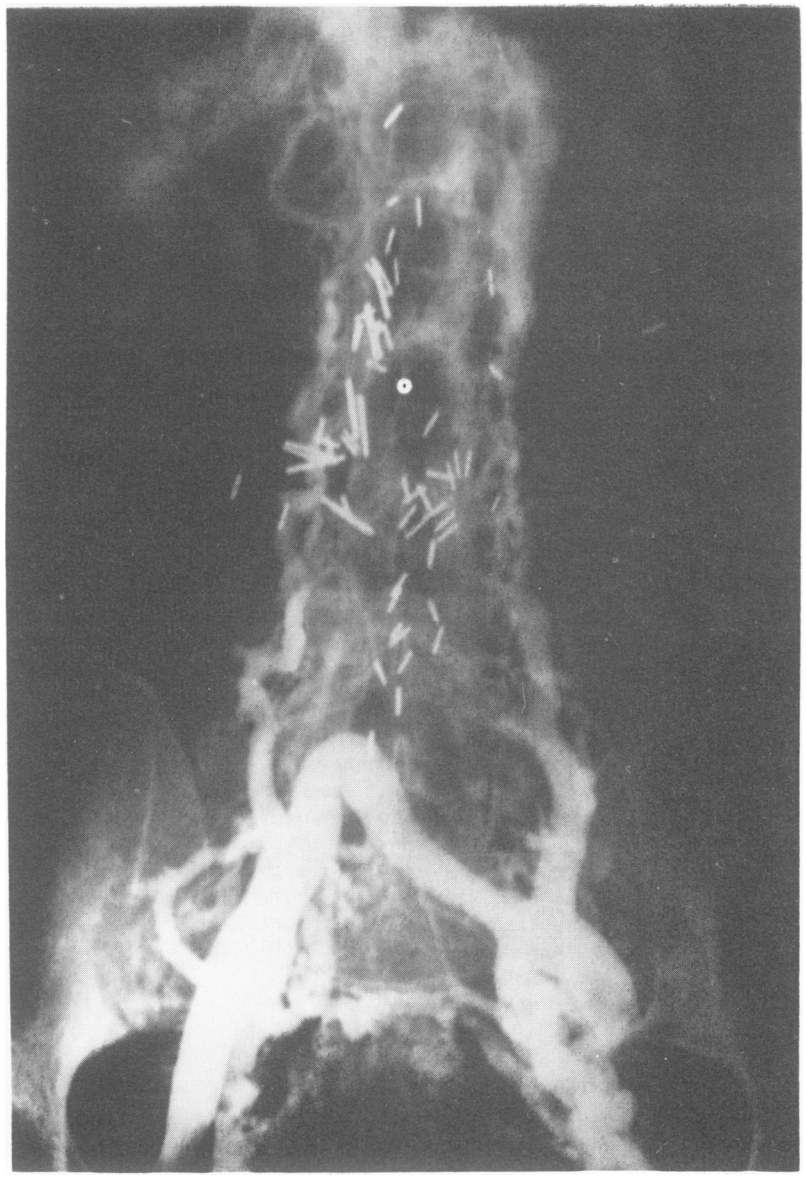
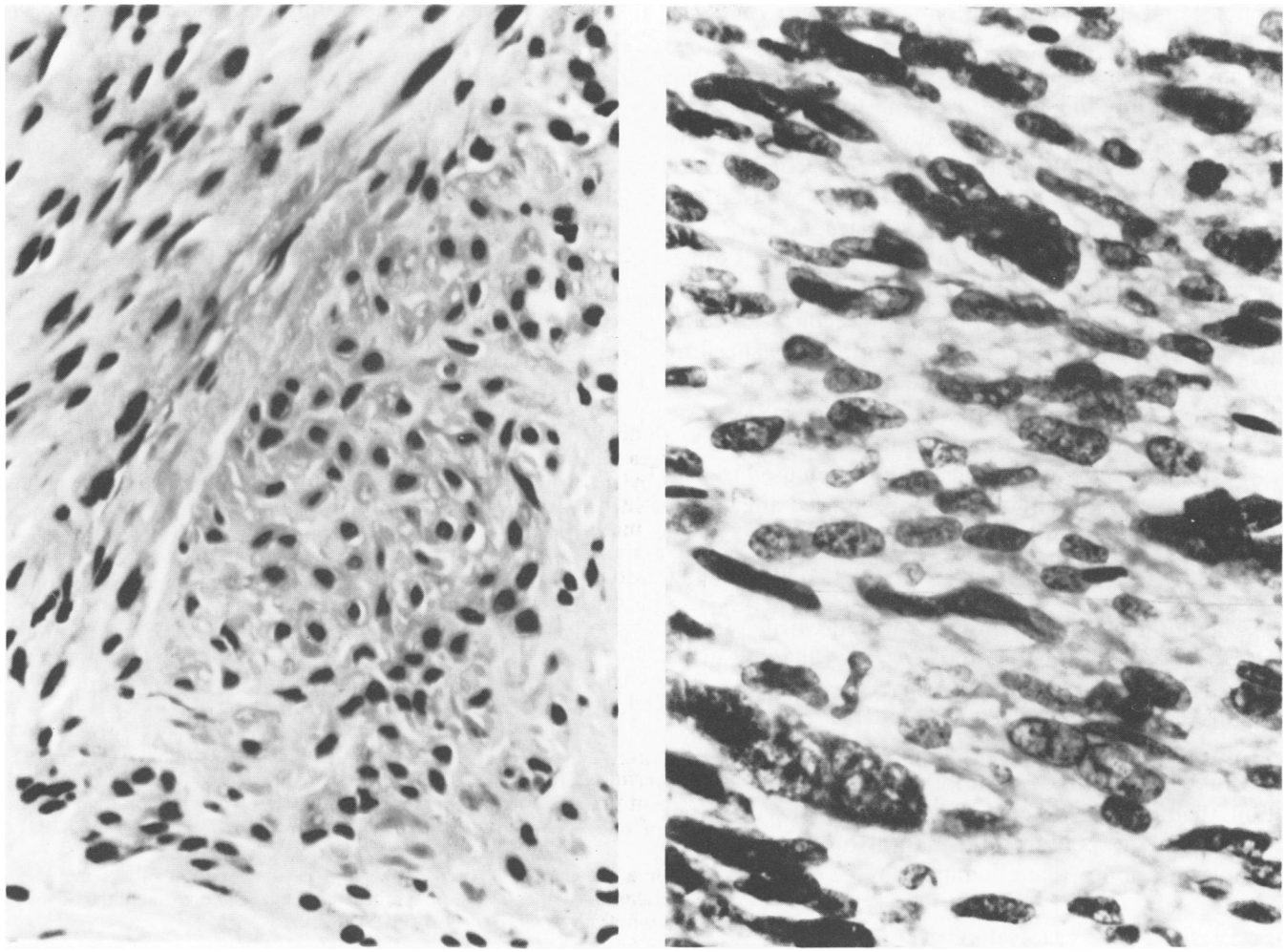


FIG. 2. Case 3—venogram demonstrating complete occlusion of composite autograft and excellent collateral circulation.

are benign or malignant from their gross appearance unless they have already demonstrated local or distal spread. Histologically, the microscopic picture can vary from the benign lesion that shows a monotonous cellular uniformity with little mitotic activity (Fig. 3a) to the highly malignant one with hypercellularity, hyperchromatism, bizarre shaped nuclei, and numerous mitoses (Fig. 3b).

Total surgical excision is the treatment of choice and is the only hope of cure for the malignant variety. At the present time, approximately 70% of such neoplasms are resectable for cure when discovered. Extirpation of the lesion should include removal of a segment of the vein from which the tumor arose and any intimately adherent surrounding nonvital structures.

Tumors arising in the inferior vena cava pose special problems depending on the location of the lesion in the vessel. Leiomyosarcomas arising in the upper one third of the inferior vena cava involving the hepatic veins are, at this time, almost always incurable. Those in the middle third, involving the renal veins, can be resected even if both renal veins are involved.[10–13] It may be necessary, in order to remove the lesion totally, to sacrifice both renal veins, in which case, right nephrectomy becomes mandatory. The left kidney will usually survive and maintain adequate function because of its excellent collateral circulation. Under unusual circumstances when the left kidney cannot maintain adequate function with renal vein interruption, either or both kidneys can be revascularized[14] or transplanted to a new vascular bed



FIGS. 3a and b. (a, left) Case 1—leiomyoma showing well defined regular bundles of spindle cells without mitoses or pleomorphism (hematoxylin = eosin, ×490). (b, right) Case 3—leiomyosarcoma showing elongated, lobulated, multinucleated giant cells with hyperchromatic, pleomorphic nuclei and mitosis. (hematoxylin = eosin, ×490).

with maintenance of an intact ureter.[11] Tumors that arise in the infrarenal portion of the vena cava (Case 3) are the most amenable to excision for cure.

An unanswered question is whether inferior vena cava reconstruction would help prevent edema of the lower extremities in those patients who do not have pre-existing edema or a history of phlebitis. Most reports in the literature recording edema after inferior vena cava ligation are related to treatment of embolic disease. Pertinent statistics are difficult to find, but a range of 33% to 38% of patients undergoing inferior vena cava ligation for pulmonary embolization who do not have pre-existing clinical evidence of phlebitis will develop mild to moderate chronic venous insufficiency and edema.[15,16] Review of the literature on vena cava ligation for septic pelvic phlebitis without iliofemoral thrombosis shows a sparcity of statistics. Collins,[17] reporting on 59 cases, indicated that there was residual long-term edema in nine (15%). It is unknown what percentage of patients who undergo caval interruption for tumor will develop edema. Review of the literature on inferior vena cava resection for vena caval, retroperitoneal, or renal neoplasms indicates a low incidence of this complication.[18,19] In only two of 13 cases (15%) in which edema status was specifically mentioned was it more than transient. This may be related to the gradual occlusion present prior to resection, with concomitant development of extensive collateral venous drainage. However, it should be noted that the incidence of residual edema is similar to that reported after inferior vena cava ligation for septic pelvic phlebitis without iliofemoral thrombosis where gradual occlusion presumably does not occur.[17]

There has been occasional attempts to reconstruct the inferior vena cava with aortic homografts,[18,20] prosthetic

grafts,[21] and the attempt with an autologous composite vein graft. To date, the authors are unaware of success by any method. Since review of the literature indicates a relatively low incidence of edema following cava resection for tumor in patients without associated thrombophlebitis or caval ligation for septic pelvic phlebitis without iliofemoral thrombosis, it is now believed that no attempt should be made at reconstruction.

The natural history of patients after resection is somewhat discouraging. Although leiomyosarcomas are slow growing, about one third of cases will recur locally after resection, and 75% of all cases will ultimately succumb to either local recurrence or distal metastases. However, long-term survival is possible (Case 2), even when attempts at curative resection have failed.

Postoperative radiation therapy has been used to treat unresectable lesions, and has also been used after resection both to prevent and/or treat recurrences. Review of available literature fails to reveal data to support success.

Chemotherapy, predominantly with doxorubicin, has also been used. Thus far, too few cases have been reported to be able to assess effect on recurrence, longevity, or survival.

Since the number of cases is small, the results of surgical resection, alone or combined with adjuvant radiation therapy and/or chemotherapy are obscure. It is hoped that by pooling information on these unusual neoplasms, appropriate therapy may be defined.

References

1. Wray RC, Dawkins H. Primary smooth muscle tumors of the inferior venae cava. Ann Surg 1971; 174:1009–1018.
2. Unruh F. In vivo diagnosticirte thrombose der venae cava inferior. Deutsche Med Wchnschr 1896; 22:746–747.
3. Melchior E. Sarkom der vena cava inferior. Deutsche Ztschr Chir 1928; 213:135–140.
4. Varela-Duran J, Oliva H, Rosai J. Vascular leiomyosarcoma. Cancer 1979; 44:1684–1691.
5. Kevorkian J, Cento DP. Leiomyosarcomas of large arteries and veins. Surgery 1973; 73:390–400.
6. Millili JJ, LaFlare RG, Nemir P Jr. Leiomyosarcoma of the abdominal aorta. Surgery 1981; 89:631–634.
7. Stringer BD. Leiomyosarcoma of artery and vein. Am J Surg 1977; 134:90–94.
8. Case records of the Massachusetts General Hospital (Case 3–1981). N Engl J Med 1981; 304:162–168.
9. Thomas MA, Fine G. Leiomyosarcoma of veins. Cancer 1960; 13:96–101.
10. Bailey RV, Stribling J, Weitzner S, Hardy JD. Leiomyosarcoma of the inferior venae cava. Ann Surg 1976; 184:169–173.
11. Brewster D, Athanasoulis CA, Darling RC. Leiomyosarcoma of the inferior venae cava. Arch Surg 1976; 111:1081–1085.
12. Turner AR. Leiomyosarcoma of the inferior venae cava. Clin Oncol 1978; 4:187–193.
13. Caplan BB, Halasz NA, Blooner WE. Resection and ligation of the suprarenal inferior venae cava. J Urol 1964; 92:25–29.
14. Wesolowski S. Un cas de resection partielle de la veine cava inferieure. J Urol med chir 1957; 63:789.
15. Donaldson MC, Wirthlin LS, Donaldson GA. Thirty-year experience with surgical interruption of the inferior vena cava for prevention of pulmonary embolism. Ann Surg 1980; 191:367–372.
16. Pollak EW, Sparks FC, Barker WF. Inferior vena cava interruption: indications and results with caval ligation, clips and intracaval devices in 110 cases. J Cardiovasc Surg 1974; 15:629–635.
17. Collins CG, Nelson EW, Ray CT, et al. Ligation of the vena cava and ovarian vessels. Am J Obstet Gynecol 1949; 58:1155–1168.
18. Crawford ES, DeBakey ME. Wide excision including involved aorta and vena cava and replacement with aortic homograft for retroperitoneal malignant tumors. Cancer 1956; 9:1085–1091.
19. Clark CD, Leeds MB. Survival after excision of a kidney, segmental resection of the vena cava, and division of the opposite renal vein. Lancet 1961; 2:1015–1016.
20. McPeak CJ. Resection of inferior venae cava and graft replacement (aortic homograft) for retroperitoneal sarcoma. Surgery 1961; 50:778–781.
21. Sarti L. Total prosthetic transplantation of the inferior vena cava, with venous drainage restoration of the one remaining kidney on the graft, successfully performed on a child with Wilm's tumor. Surgery 1970; 67:851–855.